CLAIMS

What is claimed is:

1. A method for treating erectile dysfunction in a male individual comprising administering to the individual an effective amount of a pharmaceutical composition comprising a Type V phosphodiesterase inhibitor and L-arginine.

2. The method of claim 1, wherein the Type V phosphodiesterase inhibitor is zaprinast.

3. The method of claim 1, wherein the Type V phosphodiesterase inhibitor is sildenafil.

4. The method of claim 1, wherein the Type V phosphodiesterase inhibitor is dipyridamole.

5. The method of claim 1, further comprising administering to the individual a beta blocker.

6. The method of claim 1, wherein the individual is given a daily dose of phosphodiesterase inhibitor in the range of approximately 0.001 to 100 mg/day.

7. The method of claim 1, wherein the erectile dysfunction is vasculogenic impotence.

8. The method of claim 1, wherein the phosphodiesterase inhibitor is contained within a unit dosage pharmaceutical formulation.

9. A method of inducing vasodilation or inhibiting vasospasm of a coronary artery or bypass graft comprising contacting the coronary artery or bypass graft with L-arginine and a type V phosphodiesterase inhibitor, wherein said L-arginine and said type V phosphodiesterase theinhibitor act synergistically to induce or increase vasodilation or to inhibit vasospasm of coronary artery or bypass graft.

10. The method of claim 9, wherein said L-arginine and said phosphodiestersase inhibitor are combined in a single formulation.

11. The method of claim 9, wherein the L-arginine and the phosphodiestersase inhibitor are combined with a pharmaceutically acceptable carrier.

12. The method of claim 6, wherein the phosphodiestersase inhibitor is selected from

the group consisting of zaprinast and sildenafil.

12. The method of claim 9, wherein said contacting comprises an intravenous injection of the L-arginine and the phosphodiesterase inhibitor.

13. The method of claim 9, wherein said contacting comprises an oral administration of the L-arginine and the phosphodiesterase inhibitor.

14. A pharmaceutical composition for inducing vasodilation or inhibiting vasospasm of a coronary artery or bypass graft, said composition comprising L-arginine and a type V phosphodiesterase inhibitor.

15. The composition of claim 14, further comprising a pharmaceutically acceptable carrier.

16. The composition of claim 14, wherein said type V phosphodiesterase inhibitor is selected from the group consisting of sildenafil and zaprinast.

17. In a mammal, a coronary artery or bypass graft contacted with an exogenously supplied L-arginine and an exogenously supplied phosphodiesterase inhibitor whereby said L-arginine and said phosphodiesterase inhibitor act synergistically to induce vasodilation or reducing vasospasm of said coronary artery or bypass graft.

18. In the mammal of claim 17, wherein said type V phosphodiesterase inhibitor is selected from the group consisting of sildenafil and zaprinast.

19. In the mammal of claim 17, wherein said mammal is a non-human mammal.

20. A kit for inducing vasodilation or inhibiting vasospasm of a coronary artery or bypass graft, said kit comprising one or more containers containing: L-arginine; and a type V phosphodiesterase inhibitor.

21. The kit of claim 20, further comprising a pharmaceutically acceptable carrier.

22. The kit of claim 20, wherein said type V phosphodiesterase inhibitor is selected from the group consisting of sildenafil and zaprinast.

23. A kit for treating erectile dysfunction, said kit comprising one or more containers containing: L-arginine; a type V phosphodiesterase inhibitor; and a beta blocker.

24. A method for treating a sexual dysfunction in a patient in need thereof comprising administering to the patient a therapeutically effective amount of at least one phosphodiesterase inhibitor and a therapeutically effective amount of at least one compound that stimulates endogenous nitric oxide, elevates levels of endogenous endothelium-derived relaxing factor or is a substrate for nitric oxide synthase.

25. The method of claim 24, wherein the at least one phosphodiesterase inhibitor is selected from the group consisting of sildenafil, zaprinast, dipyridamole, filaminast, piclamilast, rolipram, Org 20241, MCI-154, roflumilast, toborinone, vesnarinone, posicar, 6-bromo-1,5-dihydro-imidazo(2,1-b)quinazolin-2(3H)-one, R 79595, lixazinone, ICI 153,110, 4,5-dihydro-5-methyl-6-(4-(4-oxo-1(4H)-pyridinyl)phenyl)-3(2H)-pyridazinone, pyrazolopyrimidinones, motapizone, pimobendan, zardaverine, siguazodan, CI 930, EMD 53998, imazodan, saterinone, loprinone hydrochloride, WIN 63291, a 3-pyridinecarbonitrile derivative, denbufyllene, albifylline, torbafylline, doxofylline, theophylline, pentoxofylline, 4-((1,2-dihydro-2-oxo-6-quinolinyl)oxy)-N-ethyl-N-phenyl-butanamide, nanterinone, cilostazol, cilostamide, MS 857, WIN 62582, bentafentrine, piroximone, milrinone, amrinone, tolafentrine, dipyridamole, papaveroline, E4021, triflusal, a thienopyrimidine derivative, ICOS-351, a tetrahydropiperazino[1,2-b]beta-carboline-1,4-dione derivative, a carboline derivative, a 2-pyrazolin-5-one derivative, a fused pyridazine derivative, a quinazoline derivative, an anthranilic acid derivative, an imidazoquinazoline derivative or a pharmaceutically acceptable salt thereof.

26. The methd of claim 24, wherein the at least one phosphodiesterase inhibitor is a Type V phosphodiesterase inhibitor.

27. The method of claim 26, wherein the Type V phosphodiesterase inhibitor is sildenafil, zaprinast or dipyridamole.

28. The method of claim 24, wherein the at least one compound that stimulates endogenous nitric oxide, elevates levels of endogenous endothelium-derived relaxing factor or is a substrate for nitric oxide synthase is L-arginine, L-homoarginine, N-hydroxy-L-arginine, nitrosated L-arginine, nitrosylated L-arginine, nitrosated N-hydroxy-L-arginine, nitrosylated N-hydroxy-L-arginine, citrulline, ornithine, glutamine.or an arginase inhibitor.

29. The method of claim 24, wherein the patient is female.

30. The method of claim 24, wherein the patient is male.

31. The method of claim 24, wherein the compound that stimulates endogenous nitric oxide, elevates levels of endogenous endothelium-derived relaxing factor or is a substrate for nitric oxide synthase and the phosphodiestase inhibitor are administered orally, by intracavernosal injection, by transurethral application, or by transdermal application.

32. The method of claim 24, wherein the compound that stimulates endogenous nitric oxide, elevates levels of endogenous endothelium-derived relaxing factor or is a substrate for nitric oxide synthase and the phosphodiestase inhibitor are administered as separate pharmaceutical compositions or are administered together in the form of a single composition.

33. The method of claim 24, further comprising administering to the patient at least one vasoactive agent.

34. The method of claim 33, wherein the vasoactive agent is a potassium channel activator, a calcium blocker, an α-blocker, a β-blocker, adenosine, an ergot alkaloid, a vasoactive intestinal peptide, a dopamine agonist, an opioid antagonist, a prostaglandin, an endothelin antagonist or a mixture of two or more thereof.

35. A method for treating or preventing a disease induced by the increased metabolism of cyclic guanosine 3',5'-monophosphate in a patient in need thereof comprising administering to the patient a therapeutically effective amount of at least one phosphodiesterase inhibitor and at least one compound that stimulates endogenous nitric oxide, elevates levels of endogenous endothelium-derived relaxing factor or is a substrate for nitric oxide synthase.

36. The method of claim 35, wherein the disease induced by the increased metabolism of cyclic guanosine 3',5'-monophosphate is hypertension, pulmonary hypertension, congestive heart failure, renal failure, myocardial infarction, stable, unstable or variant (Prinzmetal) angina, atherosclerosis, cardiac edema, renal insufficiency, nephrotic edema, hepatic edema, stroke, asthma, bronchitis, chronic obstructive pulmonary disease, cystic fibrosis, dementia, immunodeficiency, premature labor, dysmenorrhoea, benign prostatic hyperplasis, bladder outlet obstruction, incontinence, a condition of reduced blood vessel patency, postpercutaneous transluminal coronary angioplasty, peripheral vascular disease, allergic rhinitis, glucoma, or a disease characterized by a gut motility disorder.

37. The method of claim 35, wherein the disease induced by the increased metabolism of cyclic guanosine 3',5'-monophosphate is a myocardial infarction; stable, unstable or variant (Prinzmetal) angina; or atherosclerosis.

38. The method of claim 35, wherein the at least one phosphodiesterase inhibitor is selected from the group consisting of sildenafil, zaprinast, dipyridamole, filaminast, piclamilast, rolipram, Org 20241, MCI-154, roflumilast, toborinone, vesnarinone, posicar, 6-bromo-1,5-dihydro-imidazo(2,1-b)quinazolin-2(3H)-one, R 79595, lixazinone, zaprinast, sildenafil, ICI 153,110, 4,5-dihydro-5-methyl-6-(4-(4-oxo-1(4H)-pyridinyl)phenyl)-3(2H)-pyridazinone, pyrazolopyrimidinones, motapizone, pimobendan, zardaverine, siguazodan, CI 930, EMD 53998, imazodan, saterinone, loprinone hydrochloride, WIN 63291, a 3-pyridinecarbonitrile derivative, denbufyllene, albifylline, torbafylline, doxofylline, theophylline, pentoxofylline, 4-((1,2-dihydro-2-oxo-6-quinolinyl)oxy)-N-ethyl-N-phenyl-butanamide, nanterinone, cilostazol, cilostamide, MS 857, WIN 62582, bentafentrine, piroximone, milrinone, amrinone, tolafentrine, dipyridamole, papaveroline, E4021, triflusal, a thienopyrimidine derivative, ICOS-351, a tetrahydropiperazino[1,2-b]beta-carboline-1,4-dione derivative, a carboline derivative, a 2-pyrazolin-5-one derivative, a fused pyridazine derivative, a quinazoline derivative, an anthranilic acid derivative, an imidazoquinazoline derivative or a pharmaceutically acceptable salt thereof.

39. The methd of claim 35, wherein the at least one phosphodiesterase inhibitor is a Type V phosphodiesterase inhibitor.

40. The method of claim 39, wherein the Type V phosphodiesterase inhibitor is sildenafil, zaprinast or dipyridamole.

41. The method of claim 35, wherein the compound that stimulates endogenous nitric oxide, elevates levels of endogenous endothelium-derived relaxing factor or is a substrate for nitric oxide synthase is L-arginine, L-homoarginine, N-hydroxy-L-arginine, nitrosated L-arginine, nitrosylated L-arginine, nitrosated N-hydroxy-L-arginine, nitrosylated N-hydroxy-L-arginine, citrulline, ornithine, glutamine or an arginase inhibitor.

42. The method of claim 41, wherein the compound that stimulates endogenous nitric oxide, elevates levels of endogenous endothelium-derived relaxing factor or is a substrate for nitric oxide synthase is L-arginine.

43. The method of claim 35, wherein the compound that stimulates endogenous nitric oxide, elevates levels of endogenous endothelium-derived relaxing factor or is a substrate for nitric oxide synthase and the phosphodiestase inhibitor are administered orally, bucally, parentally, by inhalation, by topical application, or by transdermal application.

44. The method of claim 35, wherein the compound that stimulates endogenous nitric oxide, elevates levels of endogenous endothelium-derived relaxing factor or is a substrate for nitric oxide synthase and the phosphodiestase inhibitor are administered as separate pharmaceutical compositions or are administered together in the form of a single composition.

45. The method of claim 35, further comprising administering to the patient at least one vasoactive agent.

46. The method of claim 45, wherein the vasoactive agent is a potassium channel activator, a calcium blocker, an α-blocker, a β-blocker, adenosine, an ergot alkaloid, a vasoactive intestinal peptide, a dopamine agonist, an opioid antagonist, a prostaglandin, an endothelin antagonist or a mixture of two or more thereof.

47. A pharmaceutical composition comprising a therapeutically effective amount of at least one phosphodiesterase inhibitor; at least one compound that stimulates endogenous nitric oxide, elevates levels of endogenous endothelium-derived relaxing factor or is a substrate for nitric oxide synthase; and at least one pharmaceutically acceptable carrier.

48. The pharmaceutical composition of claim 47, wherein the at least one phosphodiesterase inhibitor is a Type V phosphodiesterase inhibitor.

49. The pharmaceutical composition of claim 48, wherein the Type V phosphodiesterase inhibitor is sildenafil, zaprinast or dipyridamole.

50. The pharmaceutical composition of claim 47, wherein the compound that stimulates endogenous nitric oxide, elevates levels of endogenous endothelium-derived relaxing factor or is a substrate for nitric oxide synthase is L-arginine, L-homoarginine, N-hydroxy-L-arginine, nitrosated L-arginine, nitrosylated L-arginine, nitrosated N-hydroxy-L-arginine, nitrosylated N-hydroxy-L-arginine, citrulline, ornithine, glutamine or an arginase inhibitor.

51. The pharmaceutical composition of claim 47, wherein the compound that stimulates endogenous nitric oxide, elevates levels of endogenous endothelium-derived relaxing factor or is a substrate for nitric oxide synthase is L-arginine.

52. The pharmaceutical composition of claim 47, wherein the at least one phosphodiesterase inhibitor is selected from the group consisting of sildenafil, zaprinast, dipyridamole, filaminast, piclamilast, rolipram, Org 20241, MCI-154, roflumilast, toborinone, vesnarinone, posicar, 6-bromo-1,5-dihydro-imidazo(2,1-b)quinazolin-2(3H)-one, R 79595, lixazinone, zaprinast, sildenafil, ICI 153,110, 4,5-dihydro-5-methyl-6-(4-(4-oxo-1(4H)-pyridinyl)phenyl)-3(2H)-pyridazinone, pyrazolopyrimidinones, motapizone, pimobendan, zardaverine, siguazodan, CI 930, EMD 53998, imazodan, saterinone, loprinone hydrochloride, WIN 63291, a 3-pyridinecarbonitrile derivative, denbufyllene, albifylline, torbafylline, doxofylline, theophylline, pentoxofylline, 4-((1,2-dihydro-2-oxo-6-quinolinyl)oxy)-N-ethyl-N-phenyl-butanamide, nanterinone, cilostazol, cilostamide, MS 857, WIN 62582, bentafentrine, piroximone, milrinone, amrinone, tolafentrine, dipyridamole, papaveroline, E4021, triflusal, a thienopyrimidine derivative, ICOS-351, a tetrahydropiperazino[1,2-b]beta-carboline-1,4-dione derivative, a carboline derivative, a 2-pyrazolin-5-one derivative, a fused pyridazine derivative, a quinazoline derivative, an anthranilic acid derivative, an imidazoquinazoline derivative or a pharmaceutically acceptable salt thereof.

53. The pharmaceutical composition of claim 47, further comprising a therapeutically effective amount of at least one vasoactive agent.

54. The pharmaceutical composition of claim 53, wherein the vasoactive agent is a potassium channel activator, a calcium blocker, an α-blocker, a β-blocker, adenosine, an ergot alkaloid, a vasoactive intestinal peptide, a dopamine agonist, an opioid antagonist, a prostaglandin, an endothelin antagonist or a mixture of two or more thereof.

55. A pharmaceutical kit comprising a therapeutically effective amount of at least one phosphodiesterase inhibitor and a therapeutically effective amount of at least one compound that stimulates endogenous nitric oxide, elevates levels of endogenous endothelium-derived relaxing factor or is a substrate for nitric oxide synthase.

56. The pharmaceutical kit of claim 55, wherein the at least one phosphodiesterase inhibitor is a Type V phosphodiesterase inhibitor.

57. The pharmaceutical kit of claim 56, wherein the Type V phosphodiesterase inhibitor is sildenafil, zaprinast or dipyridamole.

58. The pharmaceutical kit of claim 55, wherein the compound that stimulates endogenous nitric oxide, elevates levels of endogenous endothelium-derived relaxing factor or is a substrate for nitric oxide synthase is L-arginine, L-homoarginine, N-hydroxy-L-arginine, nitrosated L-arginine, nitrosylated L-arginine, nitrosated N-hydroxy-L-arginine, nitrosylated N-hydroxy-L-arginine, citrulline, ornithine, glutamine or an arginase inhibitor.

59. The pharmaceutical kit of claim 55, wherein the compound that stimulates endogenous nitric oxide, elevates levels of endogenous endothelium-derived relaxing factor or is a substrate for nitric oxide synthase is L-arginine.

60. The pharmaceutical kit of claim 55, wherein the at least one phosphodiesterase inhibitor and the at least one compound that stimulates endogenous nitric oxide, elevates levels of endogenous endothelium-derived relaxing factor or is a substrate for nitric oxide synthase are separate components in the kit.

61. The pharmaceutical kit of claim 55, wherein the at least one phosphodiesterase inhibitor and the at least one compound that stimulates endogenous nitric oxide, elevates levels of endogenous endothelium-derived relaxing factor or is a substrate for nitric oxide synthase are in the form of a single composition in the kit.

62. The pharmaceutical kit of claim 55, further comprising a therapeutically effective amount of at least one vasoactive agent.

63. The pharmaceutical kit of claim 62, wherein the vasoactive agent is a potassium channel activator, a calcium blocker, an α-blocker, a β-blocker, adenosine, an ergot alkaloid, a vasoactive intestinal peptide, a dopamine agonist, an opioid antagonist, a prostaglandin, an endothelin antagonist or a mixture of two or more thereof.